


Artificial intelligence-enabled advanced endoscopic imaging to assess deep healing in inflammatory bowel disease

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ABSTRACT

Endoscopic remission is the primary long-term therapeutic goal in inflammatory bowel disease (IBD). The assessment of this therapeutic target typically relies on white light endoscopy (WLE) combined with histological sampling. Nonetheless, distinguishing between endoscopic mild, patchy inflammation and quiescent disease can be challenging, and discrepancies have been observed between endoscopic and histological disease activity, mainly when using WLE.

Recent advances in endoscopic technologies are gradually transforming clinical practice. Dye-based chromoendoscopy and virtual chromoendoscopy are currently available in the endoscopist armamentarium, enhancing the assessment of mucosal architecture and vascular patterns, improving the visualisation of patchy inflammation and helping detect subtle dysplastic colonic lesions. Moreover, novel advanced tools, including probe-based confocal laser endomicroscopy and endocytoscopy, offer the remarkable ability to investigate the deep aspect of the gastrointestinal tract in real time, including the structure and function of the intestinal barrier and inflammatory-related alterations. Thus, these techniques can bridge the gap between endoscopy and histology, enabling the integration of novel treat-to-target strategies associated with more favourable outcomes.

Artificial intelligence (AI) represents a further step forward in overcoming the limitations associated with endoscopy, including subjectivity and the requirement for expertise. Their implementation in clinical practice may enable standardised, accurate and rapid disease assessment. Moreover, AI can aid in accurately predicting responses to therapy and disease outcomes by stratifying patients' risks, thereby advancing us towards patient-centred personalised medicine.

This narrative review summarises the available advanced endoscopic technologies and their integration with AI to assess IBD activity, define promising therapeutic targets and predict long-term outcomes.

INTRODUCTION

Inflammatory bowel diseases (IBD), namely Crohn's disease (CD) and ulcerative colitis (UC), are chronic progressive inflammatory disorders characterised by a relapsing-remitting course, significantly impacting a patient's quality of life.^{1,2} The increasing global

incidence and prevalence, coupled with the highly variable disease course and response to treatment, pose significant burdens on patients and healthcare systems.²⁻⁴ Over recent years, several advanced drugs have been developed, including new biologics and novel oral small molecules, offering promising prospects to break the therapeutic ceiling in IBD, which currently stands at around 30%,⁵ and achieve long-term disease remission. However, the depth of remission to be attained remains debatable.⁶

According to the updated Selecting Therapeutic Targets in Inflammatory Bowel Disease II international guidelines, the primary long-term therapeutic goal in IBD is the achievement of endoscopic remission.^{6,7} However, there is an ongoing evolution in therapeutic targets, with a shift from endoscopic remission to emerging concepts of histological remission, transmural healing and intestinal barrier deep healing.⁸⁻¹⁰ These concepts may facilitate better patient stratification, improving long-term outcomes and enhancing disease management.

Significant advances in available endoscopic tools bolster the transition in the treat-to-target strategy. Beyond white light endoscopy (WLE), image-enhanced techniques such as dye-chromoendoscopy (DCE) and virtual chromoendoscopy (VCE) enable superior characterisation of intestinal mucosal and vascular features, aiding in the evaluation of mild inflammatory changes and early dysplastic colitis-associated lesion.¹¹⁻¹³ Additionally, advanced endoscopic tools like ultra-high magnification endocytoscopy (EC) and probe-based confocal laser endomicroscopy (pCLE) allow for a deeper assessment of the disease, challenging histology and examining the structural and molecular aspects of the intestinal barrier.¹⁴⁻¹⁶ These tools offer valuable assistance in applying novel definitions of disease healing in clinical trials and



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clinical practice, with the potential to enhance outcome prediction accuracy.

Nonetheless, the dependence on human interpretation of these endoscopic tools and related scores introduces subjectivity, high inter-observer and intra-observer variability and reliance on experts.¹⁷ Artificial intelligence (AI) is a technology that enables computers to perform tasks that typically require human intelligence. Machine learning (ML), a subset of AI, involves the development of algorithms that allow computers to learn from and make decisions based on data. These algorithms are trained on large datasets and refined through iterative processes to improve their accuracy and efficiency in performing specific tasks. In this context, AI has potential to significantly transform IBD assessment and management by accurately and objectively processing and incorporating vast amounts of data.

DISEASE HEALING IN IBD: HOW DEEP CAN WE GO?

Although the achievement of endoscopic mucosal healing is currently the recommended treat-to-target strategy in IBD, novel and deeper therapeutic goals have been proposed to achieve favourable patient outcomes (figure 1).¹⁸ Notably, the concordance between the endoscopic and histological activity severity is low ($\kappa=0.4$).¹⁹ Hence, the absence of visible endoscopic inflammation may not mirror a parallel quiescent histological activity. For this reason, a second level of mucosal healing, defined as histological healing, has been proposed. It reflects a deeper assessment of disease activity and has been demonstrated to be a reliable and accurate predictor of disease outcomes and colitis-associated neoplasia development.^{7 20–22}

Nonetheless, the assessment of histological activity still faces challenges of subjectivity and inter-rater and intra-rater variability. Furthermore, in clinical and research contexts, multiple scoring systems can be used to assess histological remission, most of which are not fully validated.²³ This accounts for high variability in histological reports and the absence of an acknowledged systematic method to define histological remission clearly.²⁴

Moving forward to endoscopy and histology, in CD, a deeper layer of healing has been proposed, that is, the transmural healing. This concept has emerged from the development of cross-sectional imaging, with intestinal ultrasound having the ability to detect transmural inflammation and accurately assess response to therapy.^{25 26}

Furthermore, delving into the concept of deep healing, the availability of endoscopic tools that allow real-time assessment of intestinal barrier structure and function has led to the introduction of intestinal barrier healing. Barrier healing showed greater ability than mucosal healing to predict major adverse outcomes (MAOs).¹⁴

Finally, the improved understanding of genomic, transcriptomic and proteomic (collectively known as OMIC) signatures of IBD will allow for the clinical implementation of molecular healing, allowing a personalised

therapeutic approach in patients with IBD in the near future.

ADVANCED ENDOSCOPY-ENHANCED IMAGING TO ASSESS MUCOSAL HEALING AND PREDICT CLINICAL OUTCOME IN IBD

The widespread adoption of HD-WLE globally underscores its status as the standard of care for routine endoscopic assessment in patients with IBD. Over the past two decades, advanced imaging techniques, including image-enhanced endoscopy and ultra-high magnification endoscopy, have gained traction in routine practice, garnering attention for accurately assessing disease activity and predicting clinical outcomes in IBD^{27 28} (figure 2).

Image-enhanced endoscopy

Image-enhanced endoscopy encompasses DCE and the evolving VCE.²⁷ DCE, using dyes such as methylene blue and indigo carmine, enhances the contrast of colonic mucosa, revealing minimal mucosal defects.²⁹ Hence, its clinical application primarily focuses on detecting cancer lesions rather than assessing IBD activity. Conversely, the use of VCE is becoming increasingly prevalent for IBD disease assessment. VCE is an electronic endoscopic imaging modality providing comprehensive contrast of the mucosal surfaces and vasculature within the colon and the rectum without dye application. VCE technology can be categorised into optical or digital variants. In optical VCE, an optical lens integrated with the endoscope's illumination source selectively filters white light to generate narrow-band light. Conversely, in digital chromoendoscopy, digital postprocessing enhances real-time images.

Various VCE technologies are currently available for clinical application, including narrow-band imaging (NBI; Olympus, Tokyo, Japan), optical enhancement iSCAN (Pentax, Tokyo, Japan), Fuji Intelligent Colour Enhancement (Fujifilm, Tokyo, Japan), Blue Laser Imaging (BLI; Fujifilm, Japan) and Linked Colour Imaging (LCI; Fujifilm Japan).²⁷ Compared with HD-WLE, VCE enables the identification of micro-inflammation and mucosal abnormalities, even when not evident with HD-WLE.^{30 31}

To standardise and accurately assess disease activity and response to therapy, Iacucci *et al*³² developed the Paddington International Virtual ChromoendoScopy ScOre (PICaSSO) using the iSCAN platform. The score distinguishes between quiescent and histological activity in UC, with a sensitivity, specificity, observed agreement and area under the receiver operating characteristic curve (AUROC) of 89.8%, 95.7%, 91.5% and 0.96%, respectively, higher than HD-WLE-based Mayo endoscopic subscore (MES). The score was successfully reproduced with the NBI and BLI/LCI platforms, showing high accuracy in predicting histological remission by Robarts Histopathology Index (RHI) and Nancy Histological Index (NHI). Furthermore, in a real-life multicentre study, the PICaSSO score predicted specified clinical outcomes at 6 and 12 months, similar to histology.

Disease Healing in IBD

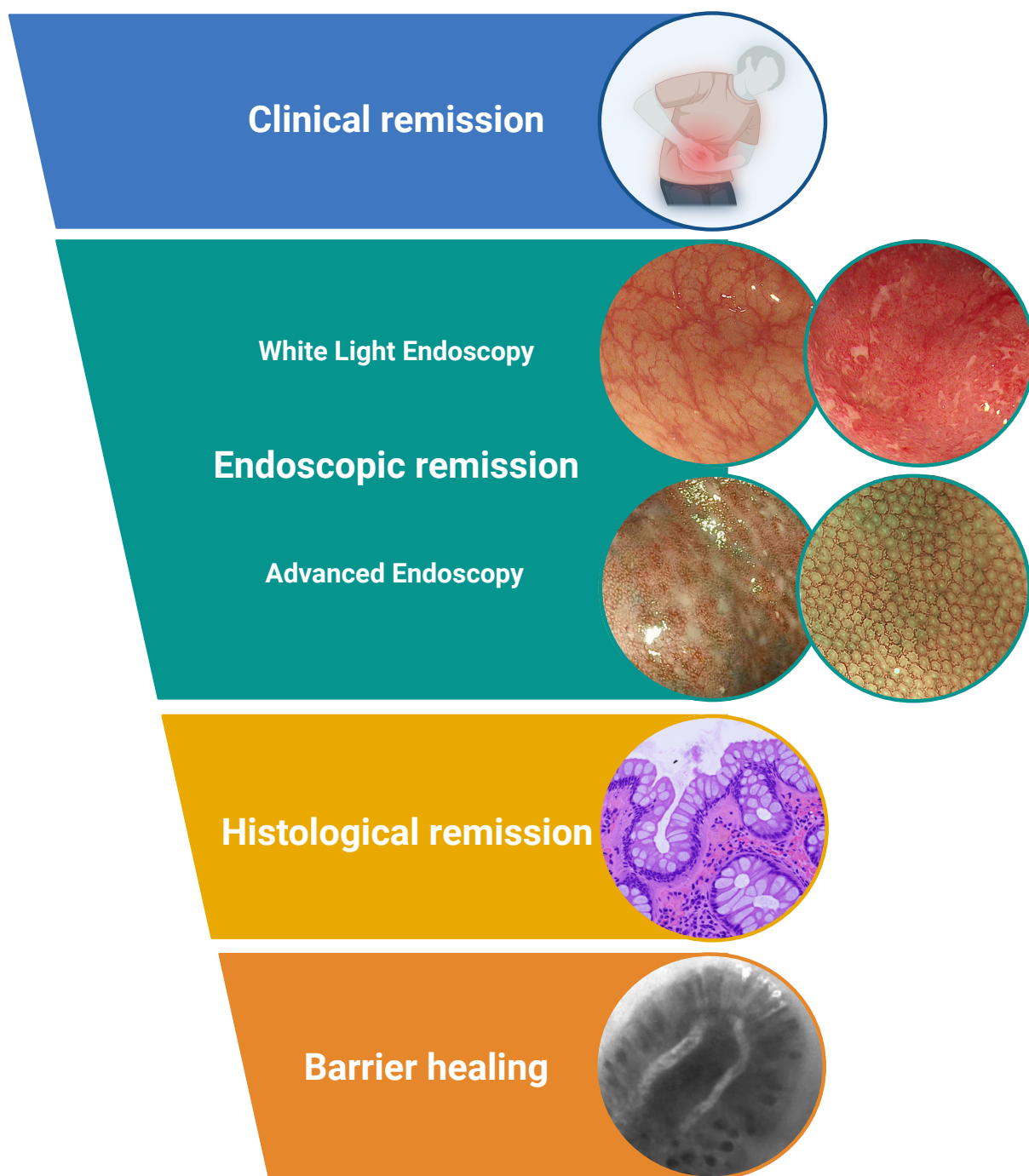


Figure 1 Different levels of disease healing in inflammatory bowel disease (IBD). Overview of the disease healing targets to achieve disease control and avoid long-term major adverse outcomes in IBD. Clinical remission: absence of IBD symptoms such as abdominal pain, diarrhoea and rectal bleeding. Endoscopic remission: absence of visible signs of inflammation in the intestinal lining during colonoscopy. Histological remission: absence of microscopic evidence of inflammation (primarily infiltration of neutrophils) in biopsy samples. Barrier healing: restoration of the intestinal barrier function, preventing harmful substances from crossing the intestinal lining. Created using BioRender.com.

Recent VCE advancements include Texture and Colour Enhancement Imaging (TXI; Olympus Japan) and Red Dichromatic Imaging (RDI; Olympus Japan). TXI

optimises the structure, colour tone and brightness of mucosal surfaces under normal light observation, aiming to improve mucosal observation by enhancing subtle

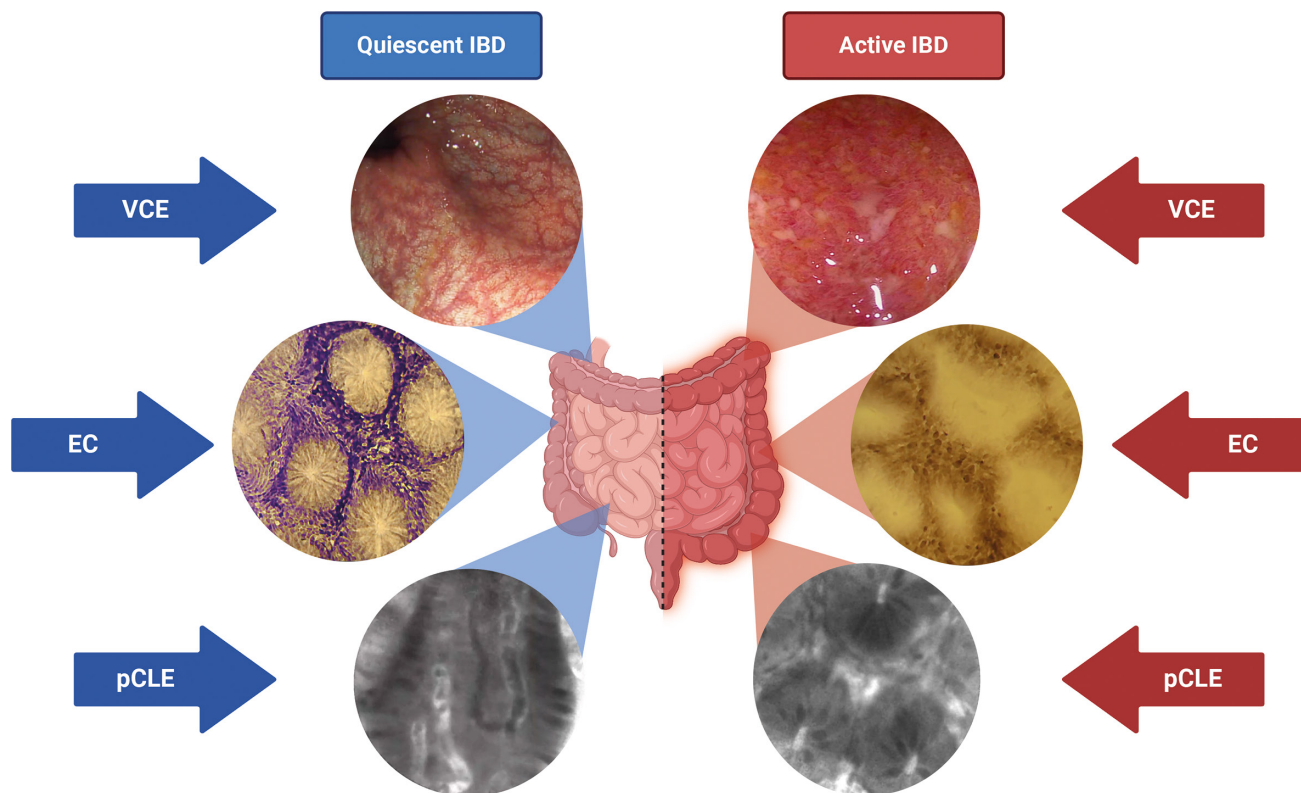


Figure 2 Advanced endoscopic techniques for assessing inflammatory bowel disease (IBD) activity. The left side of the image shows quiescent colitis, while the right side shows active disease. Images obtained by virtual electronic chromoendoscopy (VCE), endocytoscopy (EC) and probe-based confocal laser endomicroscopy (pCLE) are provided and created using BioRender.com.

changes in colour tone and structure on images that may be challenging to observe through WLE. A prospective study determined that in patients with UC classified as MES 0–1, accentuated redness and poor visibility of deep vessels at TXI represented an independent predicting factor for relapse (HR 4.2; 95% CI 1.7 to 10.0; $p < 0.01$).³³ RDI identifies deep mucosal blood vessels in patients with mild-to-moderate UC. A prospective study demonstrated that RDI scores reached a stronger correlation with histological activity (Spearman's rank r correlation coefficient of 0.63; $p < 0.01$) than WLE scores MES ($r = 0.48$) and Ulcerative Colitis Endoscopic Index of Severity (UCEIS) ($r = 0.51$).³⁴

Overall, VCE is a valuable tool for accurately assessing disease activity and response to therapy, especially in UC, and it is impressively capable of predicting outcomes. However, determining how to select among the various methods available in clinical practice represents a challenge that still needs to be addressed.

Ultra-high magnification endoscopy

Ultra-high magnification endoscopes have emerged with the concept of optical biopsy, which involves using light properties for real-time *in vivo* visualisation and evaluation of histological features. Currently, the two main ultra-high magnification endoscopic tools employed in clinical practice are EC (CF-H290ECI; Olympus, Japan) and pCLE (Cellvizio; Mauna Kea Technologies,

Paris, France).^{28–35} EC uses a 520 \times magnification microscopic lens mounted on the tip of a flexible speculum and provides colourful images through prestaining. In contrast, pCLE employs a probe with a 1000 \times magnification microscopic lens inserted through a forceps hole and presents a monochromic image.³⁶ One distinct advantage of ultra-high magnification endoscopy is the introduction of novel indicators that could not previously be observed with conventional image-enhanced endoscopy. Examples include nuclei and goblet cells with EC^{37–38} and fluorescein leakage, shedding of cells, crypt morphology and cellular infiltration with pCLE.^{28–39} These techniques enable the accurate assessment of mucosal healing and delve deeper into the evaluation of remission, advancing towards the concept of complete healing.

Endocytoscopy

Observation with EC requires prestaining with 1.0% methylene blue ($\pm 0.05\%$ crystal violet). Several scores have been introduced since its development to standardise mucosal healing assessment. In 2011, Bessho *et al* proposed a pioneering endocytoscopy scoring system (ECSS) to assess mucosal healing in UC.⁴⁰ The ECSS assesses the shape, the distance between gland lumens and the visibility of blood vessels, with a score ranging from 0 to 6. ECSS showed a strong correlation with histological activity according to Matts' score.⁴⁰ The clinical relapse rate was reported to be 7.4% (2/27) for patients

with ECSS=0 compared with 21.6% (8/37) for patients with ECSS ≥ 1 during an average follow-up period of 3 years.⁴¹

Starting from the ECSS, Iacucci *et al* proposed their ECSS. This score predicted histological remission with a sensitivity, specificity, observed agreement and AUROC of 64%, 86%, 79.5% and 0.81, respectively, allowing us to conclude that EC is a promising tool moving closer to histology.¹⁵ Furthermore, Vitali *et al* developed and prospectively validated a new endocytoscopic score (ErLangen Endocytoscopy in ColiTis score) for the in vivo assessment of microscopic disease activity. This novel and intuitive score demonstrated superiority to HD-WLE, with a sensitivity of 88%, specificity of 95.2% and AUROC of 0.92, and a strong correlation to validated histopathological scoring in predicting adverse outcomes.⁴²

As a simpler unstained EC-based indicator, microscopic vascular images obtained using NBI were proposed.^{43 44} Maeda *et al* proposed the intramucosal capillary/crypt (ICC) index to assess intramucosal vascular atypia and structural changes in the glandular lumen. During a median follow-up of 16 months in 208 patients with UC in clinical remission, they reported a relapse rate of 5.6% in patients with an ICC index ≤ 1 , compared with 30.5% in patients with an ICC index ≥ 2 ,⁴⁵ similar to stained EC observations. Furthermore, the NBI method reduced the examination time: an average of 44 s to obtain a single biopsy tissue and 130 s to take five EC images using the stained method, whereas 19 s to take five images using NBI.⁴⁵

Notably, EC's ability goes beyond the assessment of mucosal healing to the concept of barrier healing. Iacucci *et al* have recently shown that EC alone and combined with multispectral imaging analysis of intestinal barrier proteins can accurately predict adverse outcomes in IBD.⁴⁶

Probe-based confocal laser endomicroscopy

The pCLE requires administration of an intravenous fluorescein contrast and enables the assessment of the structure and function of the intestinal barrier. A first prospective study assessed small bowel epithelial gap density by pCLE, showing significantly higher barrier damage in patients with IBD than in controls ($p < 0.01$).⁴⁷ Similarly, substantially more epithelial gaps, epithelial cell shedding and fluorescein leakage have been described in the duodenal lumen of patients with IBD compared with controls, with similar changes in CD and UC.⁴⁸

Notably, Kiesslich *et al* proposed a score for barrier dysfunction in IBD based on the amount of cell shedding and the intensity of the luminal fluorescein signal. Three grades have been described, that is, normal function (grade I), functional defect (grade II) and structural defect (grade III). A Watson score II/III predicts significantly a flare-up throughout a 12-month follow-up ($p < 0.01$), with a sensitivity, specificity and observed agreement of 62.5%, 91.2% and 79%, respectively.⁴⁹

The Endoscopic Remission, Histological Remission and Barrier Healing for Predicting Disease Behaviour in IBD trial recently demonstrated that pCLE identifies barrier healing and is superior to endoscopic and histological remission for predicting MAO. Indeed, pCLE predicted MAO-free survival with an observed agreement of 72.7% in patients with UC and 88.7% in patients with CD, higher than ER (70.4% in UC and 54% in CD) or HR (66.7%–69.1% in UC and 56% in CD).¹⁴ These results paved the way for the new 'third dimension', that is, intestinal barrier healing, which could potentially be a new promising treatment target in IBD.

Delving deeper, pCLE has also been employed for molecular imaging using fluorescent antibodies, offering a potential approach to identify response to therapy in patients with IBD. Atreya *et al* developed a fluorescent antibody designed for the molecular imaging of membrane tumour necrosis factor (mTNF) in IBD. The topical administration of this antibody to 25 individuals who have CD facilitated the identification of mTNF-positive immune cells within the intestine via confocal laser endomicroscopy. Notably, subjects exhibiting elevated levels of mTNF-positive cells demonstrated a significantly enhanced short-term response rate (92%) to subsequent anti-TNF therapy at the 12-week mark, in contrast to those with lower levels of mTNF-positive cells (15%).⁵⁰ Similarly, Rath *et al*⁵¹ used molecular imaging to detect $\alpha 4\beta 7$ integrin expression in patients with CD, showing that responders to treatment had pericryptal $\alpha 4\beta 7^+$ cells compared with non-responders. More recently, Iacucci *et al* have fused pCLE with OMIC ('endo-omic approach'), going deeper into molecular healing and predicting response to therapy in IBD. They integrated computer-assisted image analysis of pCLE with RNA transcriptomics.⁵² In their study, 29 patients with IBD were enrolled to assess the predictability of their response to infliximab and vedolizumab treatments. In vivo, vessel tortuosity, crypt morphology and fluorescein leakage predicted response to therapy in both CD and UC (79% area under the curve (AUC) and 80% accuracy and 93% AUC and 85% accuracy, respectively). Moreover, ex vivo analyses showed an increased baseline binding of fluorescent-labelled biologics correlated with a greater probability of treatment success, especially in UC (83% of AUC; accuracy 77%). Furthermore, a set of differentially expressed genes, including ACTN1, CXCL6, LAMA4, EMILIN1, CRIP2, CXCL13 and MAPKAPK2, demonstrated potential in forecasting responses to anti-TNF therapy (AUROC > 0.7).

In conclusion, the ultra-high magnification endoscopy enables a real-time in vivo comprehensive dynamic assessment of disease activity and response to therapy, reaching the barrier and the molecular healing and having great potential in predicting outcomes and guiding management in patients with IBD. These studies are only performed in expert centres. Although image acquisition with these ultra-high magnification endoscopies, contact-type microscopy, is not technically difficult, training is

required to interpret the images. Additionally, the need for fluorescein and the probe's cost in pCLE are obstacles to clinical practice. An overview of the main studies investigating the role of advanced endoscopy in assessing inflammation and predicting clinical outcomes in IBD is shown in [table 1](#).

Challenges and limitations of current and advanced endoscopic techniques

Current advances in endoscopic techniques allow a detailed and enhanced evaluation of mucosal and vascular architecture of intestinal mucosa, highlighting features suggestive of subtle inflammation. However, assessing features related to disease activity and their integration into currently available scoring systems is burdened by subjectivity, high inter-observer variability and lack of knowledge and training.¹⁷ Furthermore, experts use these techniques and the related scores predominantly. A learning curve is possible in advanced endoscopic diagnostics, but it is necessary to standardise training methodologies to integrate novel diagnostic approaches into regular practice.⁵³ Moreover, the cost-effectiveness of advanced endoscopic techniques still needs to be elucidated. Finally, applying advanced endoscopic techniques is anticipated to diminish the frequency of biopsies required for inflammation evaluation. However, verifying that this reduction does not lead to an escalation in examination duration and expenses is imperative.

ROLE OF ARTIFICIAL INTELLIGENCE IN IBD

The limitations of existing endoscopic tools for assessing mucosal healing and therapeutic targets in IBD have sparked increased interest in standardising these techniques⁵⁴ for rapid, accurate and objective disease activity assessment. AI has shown promise in addressing this need, extending beyond the evaluation of mucosal healing to demonstrate good predictive ability for clinical outcomes and reaching the deeper target of histological healing⁵⁵ ([figure 3](#)). Although the journey to implementation in clinical practice remains lengthy and challenging, AI holds great potential for application in IBD.

AI-aided endoscopy for assessment healing

AI was initially applied to WLE to offer an objective and rapid assessment of disease activity, demonstrating promising potential in both UC and CD.

AI in ulcerative colitis

In 2019, Ozawa *et al* used a convolutional neural network (CNN) enhanced by deep learning techniques to innovate a computer-aided diagnosis (CAD) system that, benchmarked against expert diagnoses, was capable of accurately categorising 73%, 70% and 63% of the MES0, MES1 and MES2–3 images, respectively.⁵⁶ Concurrently, Stidham *et al* engineered a CNN model providing a four-tier classification of UC activity (MES 0–3), with commendable predictive accuracy in distinguishing

between MES.⁵⁷ Moreover, Takenaka *et al* devised a deep neural network for UC assessment, which could predict endoscopic remission with 90% accuracy.⁵⁸ Furthermore, their algorithm demonstrated a sensitivity of 92% and a specificity of 94% in predicting histological remission from endoscopic images.⁵⁸ This result was confirmed in a multicentre prospective study, where the algorithm, updated for video analysis, exhibited an enhanced sensitivity of 98% and a specificity of 95% in predicting histological remission.⁵⁹

Nonetheless, these studies relied on still images, raising concerns about selection bias. This prompted further research using videos to mitigate subjectivity and enhance the reliability of evaluations. To address this issue, Yao *et al* explored the application of their CAD system to unedited videos, developing an algorithm capable of autonomously generating a summary score for each colonoscopy.⁶⁰ Their AI model could automatically omit unsuitable images to enhance diagnostic precision. Similarly, Takenaka *et al* adapted their model to video analysis, demonstrating its ability to identify endoscopic remission correctly and strongly correlate with central reader assessments.⁵⁹

Recently, three systematic reviews and meta-analyses on this topic have been published.^{61–63} Their results revealed that the AI model demonstrated high accuracy in diagnosing endoscopic remission, as defined by both MES and UCEIS, for still images and video-based evaluations. However, these meta-analyses also showed a moderate to high heterogeneity among the targeted studies and a risk of bias. Interpretation of the results will have to await the outcomes of higher quality studies.

AI-assisted colonoscopy can also provide a more comprehensive approach to assessing the distribution of inflammation, having the ability to evaluate the patchiness of the disease and the full extent of inflammation. This approach can have significant implications for treatment choices, where understanding the full extent of inflammation is crucial. Innovations by Takabayashi *et al* and Fan *et al* have led to scoring systems considering the overall distribution of inflammation, providing a more detailed disease activity profile.^{64 65} The introduction of the Cumulative Disease Score by Stidham *et al* represents a significant leap forward. Their computer vision methods, applied to endoscopic videos from the UNIFI clinical trial, which assessed the efficacy of ustekinumab as induction and maintenance therapy in patients with UC, were able to quantify mucosal injury details better compared with MES and were more precise in discerning treatment efficacies. These results confirmed the potential of AI to significantly enhance the management of UC in both clinical trials and practice.⁶⁶ The application of AI in clinical trials extends beyond image analysis, addressing time and cost implications of endoscopic disease activity scoring. For instance, Gottlieb *et al* used data from a phase II mirikizumab trial to train and validate a CAD system autonomously scoring endoscopic severity, demonstrating high accuracy rates for endoscopic remission and promising to standardise and expedite central reading

Table 1 Overview of the main studies investigating the role of advanced endoscopy in assessing inflammation and predicting clinical outcomes

Study	Study design	Disease type	No. of patients	Aim	Outcome
Image-enhanced endoscopy					
Iacucci <i>et al</i> ³⁰	Prospective Single-centre	UC, HC	41	Diagnostic accuracy of iSCAN-OE in detecting inflammatory alterations	iSCAN-OE score accuracy to detect abnormalities: by ECAP 80% (sensitivity 78%, specificity 100%) and by RHI 68% (sensitivity 78%, specificity 50%)
Iacucci <i>et al</i> ³²	Prospective Single-centre	UC	82	Comparison of ER by modified PICaSSO (iSCAN), MES (HD-WLE) and pCLE with histological indices	Modified PICaSSO prediction of HR (RHI ≤ 3) with sensitivity, specificity, observed agreement and AUROC of 89.8%, 95.7%, 91.5% and 0.959%, respectively, higher than HD-WLE
Hayashi <i>et al</i> ³³	Prospective Single-centre	UC	146	Relapse risk of TXI score in patients with ER	TXI score 2 as risk factor for relapse ($p < 0.01$; HR 4.16)
Hashimoto <i>et al</i> ³⁴	Prospective Single-centre	UC	34	Validation of RDI score	Higher correlation to histology (NHI) than WLE scoring systems (MES, UCEIS)
EC					
Nakazato <i>et al</i> ⁴¹	Retrospective Single-centre	UC	64	Assessment of HR in patients in CR and ER	High accuracy for HR (sensitivity 0.77, specificity 0.97, diagnostic accuracy 0.86)
Iacucci <i>et al</i> ¹⁵	Prospective Single-centre	UC	29	ECSS to define ER and HR	Strong correlation with RHI ($r=0.89$) and NHI ($r=0.86$) but poor correlation with MES ($r=0.28$)
Vitali <i>et al</i> ⁴²	Prospective Single-centre	UC	46	New EC score to assess histological activity and predict clinical outcome	Strong correlation with histopathological scoring (RHI, $r=0.70$; NHI, $r=0.73$), superior to WLE and accurate prediction of clinical outcome
Maeda <i>et al</i> ⁴⁵	Retrospective Single-centre	UC	224	EC-NBI to stratify the clinical relapse risk	EC-NBI allows to stratify the risk of future clinical relapse
pCLE					
Kiesslich <i>et al</i> ⁴⁹	Prospective Single-centre	UC, CD, HC	47	Prediction of clinical relapse with pCLE scoring system	Increased scoring associated with relapse within 12 months ($p < 0.001$, with sensitivity, specificity and accuracy 62.5%, 91.2% and 79%, respectively)

Continued

Table 1 Continued

Study	Study design	Disease type	No. of patients	Aim	Outcome
Rath <i>et al</i> ¹⁴	Prospective Single-centre	UC, CD	181	Comparison of BH with ER and HR for long-term outcome prediction in patients in CR	BH superior to ER and HR to predict MAO-free survival (observed agreement 72.7% in UC and 88.7% in patients with CD)
Atreya <i>et al</i> ⁵⁰	Prospective Single-centre	CD	25	Prediction of therapeutic response to anti-TNF	High number of mTNF showed significantly higher short-term response rate
Iacucci <i>et al</i> ⁵²	Prospective Single-centre	UC and CD	29	Prediction of therapeutic response to anti-TNF and anti-integrin $\alpha 4\beta 7$	Higher mucosal binding of the drug target is associated with response to therapy in UC

AUROC, area under the receiver operating characteristic curve; BH, barrier healing; CD, Chron's disease; CR, clinical remission; EC, endocytoscopy; ECAP, extension, chronicity, activity plus; ECSS, endocytoscopy scoring system; ER, endoscopic remission; HC, healthy controls; HD-WLE, high-definition white light endoscopy; HR, histological remission; IBD, inflammatory bowel disease; LCI, linked colour imaging; MAO, major adverse outcome; MES, Mayo endoscopic subscore; mTNF, membrane tumour necrosis factor; NBI, narrow-band imaging; NHI, Nancy Histological Index; OE, optical enhancement; pCLE, probe-based confocal laser endomicroscopy; PICaSSO, Paddington International Virtual ChromoendoScopy ScOre; RDI, Red Dichromatic Imaging; RHI, Roberts Histopathology Index; TXI, Texture and Colour Enhancement Imaging; UC, ulcerative colitis; UCEIS, Ulcerative Colitis Endoscopic Index of Severity; VCE, virtual chromoendoscopy.

in clinical trials.⁶⁷ Furthermore, accurately defining the distribution of disease will allow for more precise IBD-related colorectal cancer screening intervals, potentially leading to a reduction in IBD-related colorectal cancer by ensuring timely detection and intervention.

AI in Crohn's disease

In CD, AI has been mainly applied in reading capsule endoscopy (CE), a non-invasive diagnostic technique crucial for examining the small bowel.⁶⁸ CE proves critical for evaluating disease activity, discerning mucosal inflammation and identifying complications such as strictures and fistulas. However, interpreting CE images is time-consuming and subjective, relying on physicians' expertise.

Recent years have witnessed substantial progress in the fusion of AI with CE, now capable of analysing CE images to identify mucosal lesions indicative of IBD, including ulcerations, erosions and strictures. Klang *et al* developed an AI algorithm to recognise ulcers and strictures with an AUC of 0.94 and 0.99, respectively.^{69 70} Furthermore, Majtner *et al* showed that their AI system could categorise lesions into four types—normal mucosa, aphthous ulcerations, ulcers and large ulcers/fissures—with a substantial degree of agreement with experienced gastroenterologists ($\kappa=0.72$).⁷¹ Such automated lesion detection systems can facilitate early diagnosis and monitoring of disease progression. Moreover, AI-enhanced CE holds promise for prognostic prediction, as demonstrated by Kellerman *et al*, who showed that their algorithm could predict the need for biological therapy within 6 months for patients newly diagnosed with CD, achieving an accuracy rate of

81% and an AUC of 0.86, outperforming human assessment and faecal calprotectin levels.⁷²

Finally, Brodersen *et al* undertook a multicentre investigation employing AXARO for pan-enteric CE analysis in patients with suspected CD.⁷³ Their findings indicated that observers attained a 92%–96% sensitivity and 90%–93% specificity in detecting CD, alongside a 97% sensitivity and 90%–91% specificity for IBD detection overall. The use of AXARO notably reduced the initial review duration to a median of 3.2 min.

AI-aided endoscopy enables objective and accurate assessment of mucosal healing in both UC and CD, showing potential to standardise and expedite patients' management in clinical trials and clinical practice. It holds promising abilities in disease monitoring, stratifying future relapse risk and predicting response to therapy. Table 2 summarises key studies exploring the role of AI-enabled endoscopy in assessing endoscopic healing in IBD.

AI-enabled advanced endoscopy imaging to assess histological healing

However, the development of new advanced endoscopic techniques, which enable a more accurate and deep assessment of intestinal mucosa, has prompted the application of AI to improve their evaluation of histological healing. Iacucci *et al* developed a pioneering AI-based tool that computed the PICaSSO using iSCAN videos, showing accuracies of 83%, 81% and 83% for RHI ≤ 3 , NHI ≤ 1 and PICaSSO Histological Remission Index=0, respectively.⁷⁴ Furthermore, the AI-PICaSSO model demonstrated a

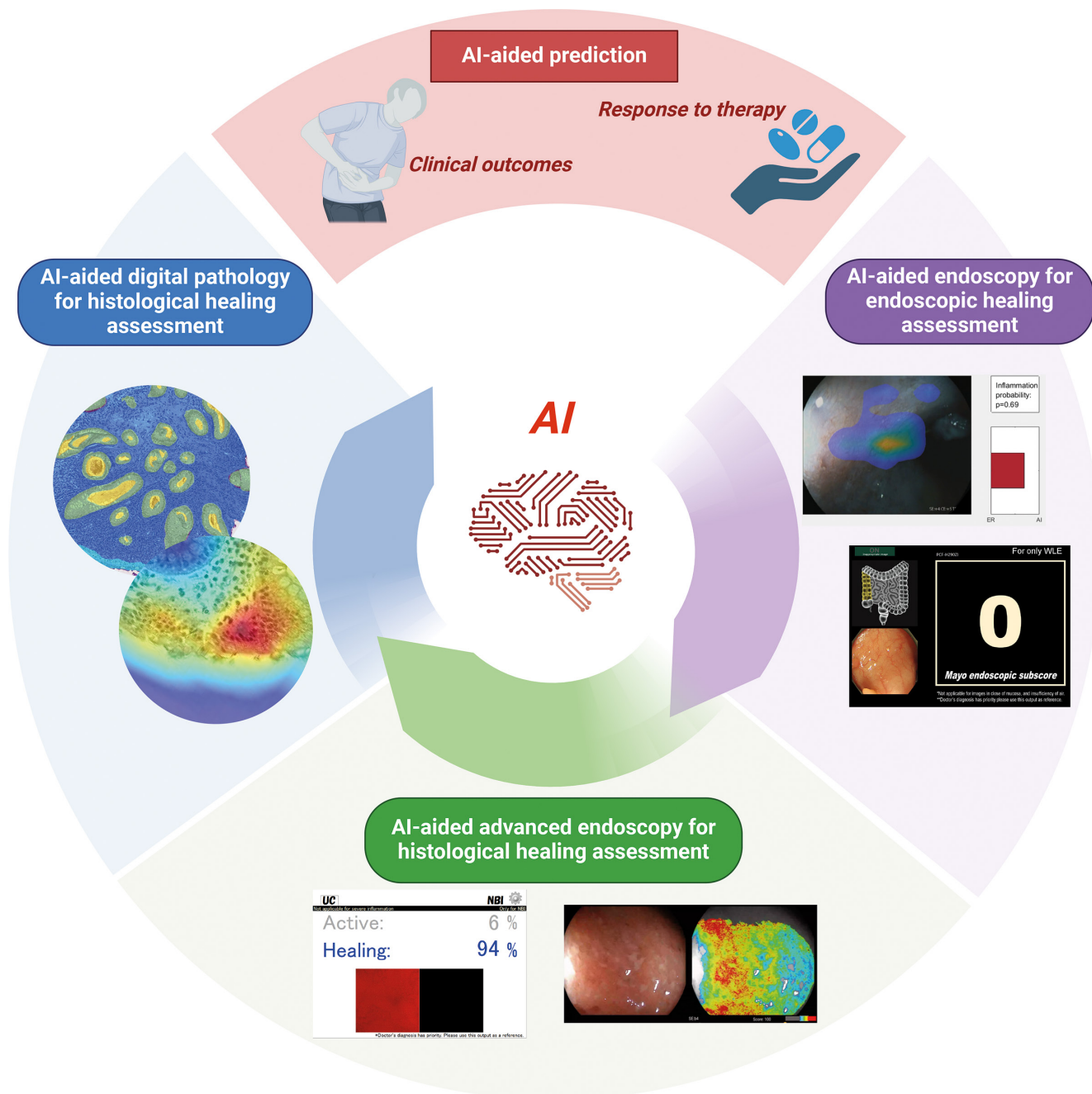


Figure 3 Artificial intelligence (AI)-enabled endoscopic and histological healing in inflammatory bowel disease (IBD). AI can aid endoscopic and histological healing objectives and accurate assessment of IBD. AI models can be applied to endoscopic videos to assist in evaluating both endoscopic and histological healing in IBD. Also, AI can be applied to histological slides to predict histological healing. AI holds the potential for predicting outcomes and responses to therapy, moving forward with personalised medicine in IBD. Examples of available AI models are provided: Paddington International Virtual ChromoendoScopy ScOre (PICaSSO) AI and AI for predicting Mayo endoscopic subscore (unpublished) on the left side of the figure; Endo-brain ulcerative colitis (UC) and red density below; PICaSSO Histological Remission Index (PHRI) AI and active learning segmentation model on the right. Image is created using BioRender.com. NBI, narrow-band imaging.

strong association between AI-based disease assessment and adverse outcomes.

Another innovative step was developing an automated diagnostic tool employing illumination from a short-wavelength monochromatic light-emitting diode (Fujifilm), enabling the real-time assessment of vascular architecture by Bossuyt *et al.* This algorithm exhibited notable efficacy, identifying histological remission with a sensitivity of 79%

and a specificity of 90%.⁷⁵ Moreover, the same group introduced the cutting-edge red density algorithm (developed by Pentax Medical, HOYA, Tokyo, Japan) to ascertain histological activity. This method leverages the red channel from RGB pixel values alongside pattern recognition in endoscopic imagery. A red density score threshold of 60 or less yielded a 96% sensitivity and 80% specificity in identifying histological remission, defined as an RHI of 6 or lower.⁷⁶

Table 2 Summary of the main studies investigating AI models to assess endoscopic remission and outcomes

Study	Study design	Objective	Modality	No. of training samples	No. of validation samples	Outcome measures	Results
Ozawa <i>et al.</i> ⁵⁶	Retrospective Single-centre	UC	WLE	26 304 images (841 pts)	3981 images (114 pts)	ER (MES=0 or 1)	AUC=0.98
Stidham <i>et al.</i> ⁵⁷	Retrospective Single-centre	UC	WLE	14 862 images (2778 pts)	1652 images (304 pts) 11 432 frames (30 videos)	ER (MES=0 or 1)	AUC=0.97 (still images) AUC=0.97 (videos)
Takenaka <i>et al.</i> ⁵⁸	Prospective Single-centre	UC	WLE	40 758 images	4187 images (875 pts)	ER (UCEIS=0) HR (Geboes <3.1)	90% accuracy for ER and 93% accuracy for HR
Takenaka <i>et al.</i> ⁵⁹	Prospective Multicentre	UC	WLE	N/A	900 segments (180 pts) 590 pts	HR (Geboes <3.1)	98% sensitivity and 95% specificity
Gottlieb <i>et al.</i> ⁶⁷	Prospective Multicentre	UC	WLE	N/A	249 videos	Grading of MES and UCIES	A quadratic weighted kappa of 0.84 for MES and 0.86 for UCEIS
Yao <i>et al.</i> ⁶⁰	Prospective Multicentre	UC	WLE	N/A	51 videos (internal data) 264 videos (external data)	ER (MES=0 or 1)	Correctly predicted the exact MES in 78% (internal data) and 57% (external data)
Takabayashi <i>et al.</i> ⁶⁴	Retrospective Multicentre	UC	WLE	14 208 images	1479 images	The correlation coefficients between IBD expert endoscopists and the AI	Spearman's correlation coefficients were all higher than 0.95 (p<0.01)
Fan <i>et al.</i> ⁶⁵	Retrospective Single-centre	UC	WLE	5875 images (332 pts)	20 full-length videos (18 pts)	Grading of MES and single UCEIS items in WLE	86.5% accuracy in the MES (κ=0.81), UCEIS items with accuracies of 90.7%, 84.6% and 77.7% for vascular pattern (κ=0.82), erosions and ulcers (κ=0.78) and bleeding (κ=0.70)
Stidham <i>et al.</i> ⁶⁶	Prospective Multicentre	UC	WLE	N/A	748 pts	Cumulative Disease Score performance	Cumulative Disease Score had better sensitivity for detecting endoscopic changes than MES

Continued

Table 2 Continued

Study	Study design	Objective	Modality	No. of training samples	No. of validation samples	Outcome measures	Results
Klang <i>et al</i> ⁶⁹	Retrospective Single-centre	CD	CE	17 640 images from 49 pts with CD	Cross-validation	The detection abilities of small-bowel ulcers	Accuracies ranging from 95.4% to 96.7%
Klang <i>et al</i> ⁷⁰	Retrospective Single-centre	CD	CE	27 892 images; 1942 strictures images, 14 266 normal mucosa images and 11 684 ulcer images	Cross-validation	The classifying strictures versus non-strictures	93.5% accuracy
Majtner <i>et al</i> ⁷¹	Retrospective Single-centre	CD	CE	70% images of 7744 images from 38 pts	20% images of 7744 images from 38 pts	The identification of ulcerations	95.7% sensitivity, 99.8% specificity and 98.4% accuracy
Kellerman <i>et al</i> ⁷²	Retrospective Multicentre	CD	CE	101 pts	Cross-validation	The prediction of the need for biological therapy	81% accuracy
Brodersen <i>et al</i> ⁷³	Prospective Multicentre	CD	CE	N/A	131 suspected CD pts	The identification abilities of CD and IBD	92%–96% sensitivity and 90%–83% specificity for CD and 97% sensitivity and 90%–91% specificity for IBD

AI, artificial intelligence; AUC, area under the curve; CD, Crohn's disease; CE, capsule endoscopy; ER, endoscopic remission; HR, histological remission; IBD, inflammatory bowel disease; MES, Mayo endoscopic subscore; N/A, not available; NHI, Nancy Histological Index; PHRI, PICAISO Histological Remission Index; PICAISO, Paddington International Virtual ChromoendoScopy ScOre; pts, patients; RHI, Roberts Histopathology Index; UC, ulcerative colitis; UCEIS, Ulcerative Colitis Endoscopic Index of Severity; WLE, white light endoscopy.

Noteworthy is the first CAD system by Maeda *et al* applied to EC, which showed a sensitivity of 74% and a specificity of 97% in predicting histological remission.⁷⁷ Further research demonstrated that AI-enabled real-time EC could stratify the clinical relapse risk in patients with UC in clinical remission. The AI analysis categorised the patients into two cohorts: those with AI-detected active disease and those with AI-detected healing. The cohort of 134 patients was monitored prospectively for 12 months after colonoscopy.⁷⁸ Clinical relapse occurred in 28.4% (21 out of 74) of the subjects within the AI-detected active disease cohort, in contrast to 4.9% (3 out of 61) in the AI-detected healing cohort ($p=0.01$). A novel iteration of this CAD system, designated as EndoBRAIN-UC (Cybernet Systems, Tokyo, Japan), obtained regulatory approval in Japan and has been available for commercial purchase since February 2021. Omori *et al* confirmed the efficacy of the market-ready EndoBRAIN-UC in an external validation cohort, showing a sensitivity of 74.2% and a specificity of 93.8% for diagnosing histological remission.⁷⁹

Nonetheless, the application of EndoBRAIN-UC is restricted to the experts who operate the ultra-high magnification endoscope. Addressing this challenge, Kuroki *et al* unveiled an ancillary system compatible with a more inclusive array of endoscopes, capable of rendering an objective dichotomous diagnosis of either 'AI-based vascular healing' or 'AI-based vascular activity'.⁸⁰ Their findings indicated a significantly higher occurrence of clinical relapse within 12 months postcolonoscopy in patients diagnosed with AI-based vascular activity (23.9% (16/67)) compared with those diagnosed with AI-based vascular healing (3.0% (1/33)) ($p=0.01$).

Regarding pCLE, pioneering computer-based models have been developed, showing the promising ability to assess mucosal healing by evaluating crypts, vessel architecture and fluorescein leakage.⁸¹ Furthermore, as previously discussed, Iacucci *et al* developed a computer-aided imaging analysis of pCLE, which had a promising ability to predict response to biological therapy in patients with IBD.⁵²

In summary, AI-enhanced advanced endoscopy can objectively assess more deep levels of healing in IBD, reach histological remission and predict outcomes. This approach can revolutionise precision medicine for patients with IBD. Table 3 shows an overview of the main studies investigating the role of AI-aided advanced endoscopy in assessing histological remission and predicting clinical outcomes in IBD.

AI-enabled digital pathology to assess histological healing

The role of AI in assessing mucosal healing in IBD extends beyond its application in endoscopy and has demonstrated significant promise when applied to histology. Similarly to endoscopy, the scores commonly used to grade histological disease activity in IBD are complex and burdened by high inter-observer variability.⁸² Validated scoring systems and standardised reporting have been widely

encouraged, especially in randomised clinical trials.⁸³ However, the lack of training and knowledge about available scoring systems makes disease assessment extremely subjective and challenging even within this framework. AI has the potential to revolutionise this field as well, and one crucial step in its implementation in clinical trials and practice was the incorporation of digital slides into whole-slide imaging (WSI). This transformation allows the digitisation of glass slides with tissue specimens into high-resolution images for computer-assisted viewing and analysis, enabling the application of advanced computer vision techniques.⁸⁴

Vande Casteele *et al* introduced the first deep learning algorithm for identifying eosinophils, which indicates active UC. This algorithm, trained on manually annotated eosinophils from digitised colonic biopsy images, showed exceptional concordance with traditional eosinophil counts by pathologists, as evidenced by intraclass correlation coefficients ranging from 0.81 to 0.92.⁸⁵ Similarly, Ohara *et al* employed a deep learning model to measure the goblet cell mucus area ratio in histological images from patients with UC in remission.⁸⁶ This innovative approach highlighted the potential of the rectal goblet cell ratio as a marker for UC activity and a predictor of clinical relapse risk.

The detection of neutrophils, a marker of disease activity, has been a focal point of AI research in histology. The PICaSSO group introduced CNNs to identify neutrophils in WSI, effectively categorising histological remission or active disease with 78% sensitivity, 91.7% specificity and 86% accuracy.⁸⁷ Following this, the team developed a CAD system with proven efficacy in recognising UC disease activity across various histological indices and forecasting clinical outcomes. It demonstrated robust diagnostic capabilities, rivalling those of human pathologists, in assessing histological activity and remission and predicting 12-month flare risks.⁸⁸ Similarly, Peyrin-Biroulet *et al* show the utility of a ML model applied to histopathology to assign a scoring based on the NHI, resulting in the performance of the ML tool being equivalent to that of experienced histopathologists: 89.3 of the average intraclass correlation coefficients among the histopathologists vs 87.2 of the average intraclass correlation coefficients between histopathologists and the ML tool.⁸⁹ More recently, Rymarczyk *et al* explored AI models to automate UC histological disease activity assessment in histological slides from phase II and phase III clinical trials. These models, trained on extensive imaging data from clinical trials, showed proficiency in predicting Geboes histopathology scores for UC and Global Histology Activity Score for CD.⁹⁰

Another potential application of AI in histology is predicting response to therapy. Liu *et al* elucidate an innovative methodology for merging ML algorithms-based WSI to predict treatment efficacy in paediatric UC, pinpointing individuals likely to attain steroid-free remission solely through mesalamine treatment.⁹¹ The ML model underwent training using 187571 informative

Table 3 Summary of the main studies investigating AI-assisted endoscopy models to assess histological remission and outcomes

Study	Study design	Objective	Modality	No. of training samples	No. of validation samples	Outcome measures	Results
Takenaka et al ⁶⁹	Prospective Multicentre	UC	WLE	N/A	900 segments (180 pts) 590 pts	HR (Geboes <3.1)	98% sensitivity and 95% specificity
Iacucci et al ⁷⁴	Prospective Multicentre	UC	iSCAN	67 280 frames (283 pts)	242 videos	ER (UCEIS ≤1 and PICaSSO ≤3) HR (RHI ≤3, NHI ≤1 and PHRI ≤1)	ER of UCEIS ≤1 with a sensitivity of 72%, specificity of 87% and PICaSSO ≤3 with a sensitivity of 79%, specificity of 95%. Accuracies of HR ranging from 80% to 85%
Bossuyt et al ⁷⁵	Prospective Single-centre	UC	Single short-wavelength monochromatic LED illumination	N/A	113 segments (58 pts)	HR (Geboes <2B.1)	79% sensitivity and 90% specificity
Bossuyt et al ⁷⁶	Prospective Multicentre	UC	Red density algorithm	N/A	29 pts with UC and 6 healthy controls	Correlation of red density score with RHI, MES and UCEIS	Red density score correlated with RHI (r=0.74), MES (r=0.76) and UCEIS (r=0.74)
Maeda et al ⁷⁷	Retrospective Single-centre	UC	Endocytoscope-NBI	12 900 images (87 pts)	525 segments (100 pts)	HR (Geboes <3.1)	74% sensitivity and 97% specificity
Maeda et al ⁷⁸	Prospective Single-centre	UC	Endocytoscope-NBI	44 097 images	135 pts	Clinical relapse during 12 months after colonoscopy	The relapse rate was significantly higher in the AI-active group (28%) than in the AI-healing group (5%; p<0.001)
Omori et al ⁷⁹	Retrospective Single-centre	UC	Endocytoscope-NBI	N/A	191 segments (52 pts)	HR (Geboes <3.1)	74.2% sensitivity and 93.8% specificity
Kuroki et al ⁸⁰	Prospective Single-centre	UC	NBI	8853 images (167 pts)	104 pts	Clinical relapse during 12 months after colonoscopy	The relapse rate was significantly higher in the vascular-active group (24%) than in the vascular-healing group (3%; p<0.001)
Queenhervet al ⁸¹	Retrospective Single-centre	UC and CD	CLE	N/A	59 pts	Computer-based analysis of CLE images to characterise IBD	Discrimination of UC from CD 92% sensitivity and 91% specificity

Continued

Table 3 Continued

Study	Study design	Objective	Modality	No. of training samples	No. of validation samples	Outcome measures	Results
Iacucci et al ⁵²	Prospective Single-centre	UC and CD	CLE	N/A	29 pts	The predictability of their response to infliximab and vedolizumab treatments	83% of AUC; accuracy 77%
AI, artificial intelligence; AUC, area under the curve; CD, Crohn's disease; CLE, confocal laser endomicroscopy; ER, endoscopic remission; IBD, inflammatory bowel disease; ICC, interclass correlation coefficient; MES, Mayo endoscopic subscore; N/A, not available; NBI, narrow-band imaging; NHI, Nancy Histological Index; PHRI, PICA SSO Histological Remission Index; PICA SSO, Paddington International Virtual ChromoendoScopy ScOre; pts, patients; RHI, Roberts Histopathology Index; UC, ulcerative colitis; UCEIS, Ulcerative Colitis Endoscopic Index of Severity; WLE, white light endoscopy.							

patches extracted from rectal H&E-stained biopsy specimens collected from 292 treatment-naïve paediatric patients with UC within a multicentric inception cohort investigation. Conclusively, the authors verified that an ensemble of 18 histomic features maintained consistent performance in an independent real-world external cohort, achieving an AUC of 0.85 at the WSI level in predicting requirement of biological therapy during 12 months.

Therefore, the application of AI in histology holds significant promise in IBD for assessing histological remission, forecasting outcomes and response to therapy, as shown in [table 4](#). Yet, what is particularly encouraging is the prospect of AI integrating endoscopy, histology and OMICs, known as the endo-histo-OMIC approach, to thoroughly assess patients with IBD, marking the advent of a new era in IBD personalised medicine.⁸⁴

CHALLENGES AND FUTURE PERSPECTIVES OF AI IN CLINICAL PRACTICE

AI-based algorithms can systematically and objectively evaluate endoscopic and histological mucosal inflammation, predict long-term outcomes, and ultimately guide disease management toward patient-centred personalised medicine.^{92 93} In this context, AI stands poised to enhance this process under the watchful guidance of physicians, having the extraordinary ability to integrate large datasets encompassing clinical data, endoscopic and histological findings and OMIC data, thereby providing profound insights into the intricacies of IBD.

The application of AI to advanced endoscopy and histology holds immense promise in revolutionising the management of IBD by facilitating objective and rapid assessment of mucosal healing and enabling outcome prediction. While numerous AI-related studies have proliferated in scientific research, only a handful of them have secured regulatory approval, resulting in limited clinical adoption. Most cited articles in the manuscript are studies conducted in expert academic centres with minimal real-world validation. The development and validation data were also collected from the same facility, raising concerns about sampling bias. External validation in different facilities and with different endoscopists is needed to determine the performance and robustness of AI systems. To introduce AI in endoscopy into routine clinical practice, the IBD academic community, in collaboration with industry, should consider developing more 'real-world' IBD datasets from non-expert or community practices. This gap underscores the need for robust empirical validation, as doubts persist regarding AI's real-world accuracy, and indeed, several challenges must be addressed to facilitate AI-based technologies implementation in clinical practice. One key challenge is ensuring the reliability and robustness of AI algorithms, as variations in data quality and sources can impact their

Table 4 Summary of the main studies investigating AI-aided digital pathology models to assess histological remission and outcomes

Study	Study design	Objective	Modality	No. of training samples	No. of validation samples	Outcome measures	Results
Vande Castele <i>et al</i> ⁸⁵	Retrospective Single-centre	UC	WSI	88 pts	20 tissue regions	Identification of eosinophil counts	Almost perfect agreement with four pathologists (ICCs: 0.81–0.92)
Ohara <i>et al</i> ⁸⁶	Retrospective Single-centre	UC	WSI	2300 images	114 pts	Automated calculation of goblet cell ratio, and prediction of clinical relapse	Pts with a GCR (the ratio of goblet cell mucus area to the epithelial cell and goblet cell mucus area) of $\leq 12\%$ had a significantly higher relapse rate than those with a GCR of $>12\%$ (45% vs 6.5%; $p < 0.01$)
Gui <i>et al</i> ⁸⁷	Prospective Multicentre	UC	WSI	97 biopsies	41 biopsies	HR (PHRI < 1)	78% sensitivity, 91.7% specificity and 86.0% accuracy
Iacucci <i>et al</i> ⁸⁸	Prospective Multicentre	UC	WSI	118 biopsies	A: 375 biopsies B: 154 biopsies (58 pts)	A: HR (PHRI ≤ 1 , RHI ≤ 3 and NHI ≤ 1) B: prediction of prognosis	Sensitive and specific at 89% and 85% (PHRI), 94% and 76% (RHI) and 89% and 79% (NHI). B: the HR for disease flare-up was 4.6
Peyrin-Biroulet <i>et al</i> ⁸⁹	Retrospective Single-centre	UC	WSI	160 biopsies	40 biopsies	The correlation between histopathologists and the AI for diagnosing NHI	The average ICC was 87.2
Rymarczyk <i>et al</i> ⁹⁰	Retrospective Multicentre	UC and CD	WSI	2696 biopsies	800 biopsies	Grading of Geboes score determined by experts	Accuracy was 65%–85% (k range: 0.44–0.68)
Liu <i>et al</i> ⁹¹	Retrospective Multicentre	Paediatric UC	WSI	187 571 patches from 292 biopsies	113 pts	The predicting requirement of biological therapy during 12 months.	AUC of 0.85 at the WSI level

AI, artificial intelligence; AUC, area under the curve; CD, Crohn's disease; HR, histological remission; IBD, inflammatory bowel disease; ICC, interclass correlation coefficient; NHI, Nancy Histological Index; PHRI, PICaSSO Histological Remission Index; pts, patients; RHI, Roberts Histopathology Index; UC, ulcerative colitis; WSI, whole-slide imaging.

performance. This is because humans train datasets for developing AI algorithms and are, therefore, susceptible to biases. To mitigate this, ongoing validation and refinement of AI models are essential, with clear study designs, alongside the development of standardised data collection and analysis protocols. Another critical issue is the reproducibility of AI-enabled findings, necessitating rigorous validation through randomised controlled trials to demonstrate their clinical utility and effectiveness. Referencing computer diagnosis systems for colorectal lesions, it has been reported that AI can enhance the ability to differentiate neoplasia from non-neoplasia.⁹⁴ However, some randomised controlled trials and meta-analyses have shown no incremental benefit.^{95 96} In IBD-related AI in endoscopy, Ogata *et al* most recently showed that using AI improves diagnostic accuracy and intra-reproducibility and inter-reproducibility of non-specialists for scoring MES.⁹⁷ However, the analysis was based on prerecorded videos and has not been validated in real time. We should further evaluate the human-endoscopist-AI interaction component that will likely critically impact AI outputs.

To accelerate the resolution of these issues, it is hoped that within a few years, multiple AI products for IBD endoscopy will be approved by regulatory authorities and become available for routine clinical use. Initially, the introduction may not be as ideal as hoped; however, understanding human-AI interaction would enable using these tools more effectively and as standard practice. Additionally, discrimination and data privacy concerns must be addressed to uphold ethical standards and protect patient confidentiality. Moreover, patient safety issues related to AI malfunctioning and legal implications for malpractice must be explored in the future. Establishing international guidelines and AI-working groups will overcome these concerns and regulate the use of AI.

Implementing transparent algorithms, robust data governance frameworks and ensuring compliance with regulatory guidelines can help mitigate these concerns and foster trust among patients and healthcare providers. This trust will be crucial for effectively accepting AI into everyday clinical care. By tackling these challenges head-on and implementing appropriate solutions, AI-enabled technologies can realise their full potential in transforming IBD management and improving patient outcomes. Although some challenges remain to be addressed and the path to clinical implementation is still long and tortuous, these innovative tools hold promise in realising the vision of precision medicine in IBD.

Integrating advanced endoscopic tools with AI presents a transformative potential within the realm of IBD. Their main strength lies in their capacity to accurately assess the primary therapeutic goals, from endoscopic healing to delving deeper into histological and deep healing. This has the potential to revolutionise

clinical trials and practice, fundamentally improving the management of patients with IBD.

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